

Claims:

1. A chimeric antibody conjugate comprising an antigen binding region of a non-human antibody and an immunoglobulin constant region which
 5 comprises at least one C_H domain ~~or epitope thereof~~, with the proviso that the constant region is not a naturally occurring F_C fragment.
2. A chimeric antibody conjugate according to claim 1 in which the
 10 non-human antigen binding region comprises or consists of a non-human Fab fragment or part thereof.
3. A chimeric antibody conjugate according to claim ^{claim 1} ~~1 or claim 2~~ in
 15 which the non-human antigen binding region comprises or consist of an scFv fragment.
4. A chimeric antibody conjugate according to ^{claim 1} ~~any one of claims 1 to 3~~
 in which the non-human antigen binding region is derived from a mouse.
5. A chimeric ~~antibody~~ conjugate according to ^{claim 1} ~~any one of claims 1 to 4~~
 20 in which the constant region is derived from a human antibody.
6. A chimeric ~~antibody~~ conjugate according to ^{claim 1} ~~any one of claims 1 to 5~~
 25 in which the constant region comprises one or more constant domains derived from an IgM antibody.
7. A chimeric ~~antibody~~ conjugate according to claim 6 in which the
 constant region **comprises one** or more C_H3μ domains.
8. A chimeric ~~antibody~~ conjugate according to ^{claim 1} ~~any one of claims 1 to 5~~
 30 in which the constant region comprises one or more constant domains derived from an IgG antibody.
9. A chimeric antibody conjugate according to claim 8 in which the
 35 constant region comprises one or more C_H3γ domains.

a 10. A chimeric antibody conjugate according to ^{Claim 1}~~any one of claims 1 to 5~~ in which the constant region comprises one or more constant domains derived from an IgA antibody.

a 5 11. A chimeric antibody conjugate according to ^{Claim 1}~~any one of claims 1 to 10~~ in which the constant region comprises a non-naturally occurring combination of C_H domains or epitopes thereof.

a 10 12. A chimeric antibody conjugate according to ^{Claim 1}~~any one of claims 1 to 11~~ in which the non-human antigen binding region binds to an epitope of an infectious agent selected from dengue virus, rubella virus, herpes virus, parvovirus, human glycoporphin, *Rickettsia sibirica*, *Burkholderia pseudomallei*, *Salmonella typhi* or *paratyphi*, *Leptospira interrogans*, *Plasmodium falciparum/vivax*, Japanese encephalitis virus, Yellow fever virus, *Bordetella pertussis/parapertussis*, *Candida albicans/kruzei*, Varicella zoster virus, HIV, 15 Hepatitis viruses, Human papilloma virus, Epstein-Barr virus, Ross River virus, *Brucella abortis*, Human herpesvirus-6, Parvovirus B19, *Coxiella burnettii*, Herpes simplex viruses 1&2, *Rickettsia rickettsii*, *Conori australis*, and *Rickettsia tsutsugamushi*.

20 13. A recombinant polynucleotide molecule comprising a sequence encoding a non-human V_H region, a sequence encoding a non-human V_L region, a sequence encoding a flexible linker positioned between the V_H region sequence and the V_L region sequence, and a heterologous sequence 25 encoding a C_H domain or epitope thereof.

14. A recombinant polynucleotide molecule according to claim 13 in which the heterologous sequence encodes a human C_H domain.

a 30 15. A recombinant polynucleotide molecule according to claim 13 ~~or claim 14~~ in which the C_H domain sequence is linked to the 3' end of the V_L or V_H sequence.

a 35 16. A recombinant polynucleotide molecule according to ^{Claim 13}~~any one of claims 13 to 15~~ in which the polynucleotide molecule includes a control

sequence which directs the synthesis of both the V_L and V_H polypeptide regions.

17. A recombinant polynucleotide molecule according to claim 16 in which the control sequence is the lac promoter.

18. A recombinant polynucleotide molecule according to ^{claim 13} ~~any one of claims 13 to 17~~ in which the molecule includes a sequence encoding a leader peptide which directs the synthesised polypeptide chains to the host cell periplasm.

19. A recombinant polynucleotide molecule according to claim 18 in which the leader sequence is the pel B sequence.

20. A recombinant polynucleotide molecule comprising a sequence encoding a non-human V_L region, a sequence encoding a non-human C_L region, a sequence encoding a non-human V_H region, a heterologous sequence encoding a C_H domain or epitope thereof, and optionally a sequence encoding a non-human C_{H1} region.

21. A recombinant polynucleotide molecule according to claim 21 in which the heterologous sequence encodes a human C_H domain.

22. A recombinant polynucleotide molecule according to claim 20 ~~or claim 21~~ in which the V_L and C_L sequences are linked together so that the V_L and C_L regions are expressed as a single polypeptide.

23. A recombinant polynucleotide molecule according to ^{claim 20} ~~any one of claims 20 to 22~~ in which the V_H and C_{H1} sequences are linked together so that the V_H and C_{H1} regions are expressed as a single polypeptide.

24. A recombinant polynucleotide molecule according to ^{claim 20} ~~any one of claims 20 to 23~~ in which the polynucleotide molecule includes a control sequence which directs the synthesis of both the V_L-C_L and V_H-C_{H1} polypeptide regions.

25. A recombinant polynucleotide molecule according to claim 24 in which the control sequence is the lac promoter.

a 26. A recombinant polynucleotide molecule according to ^{Claim 20} ~~any one of~~
5 ~~claims 20 to 25~~ in which the polynucleotide molecule includes a sequence encoding a leader peptide which directs the synthesised polypeptide chains to the host cell periplasm.

27. A recombinant polynucleotide molecule according to claim 26 in
10 which the leader sequence is the pel B sequence.

a 28. A recombinant polynucleotide molecule according to ^{Claim 20} ~~any one of~~
a ~~claims 20 to 27~~ in which the heterologous C_H domain sequence is linked to
15 the V_L-C_L sequences or the V_H-C_H1 sequences so that the expressed heterologous C_H domain is attached to the V_L-C_L polypeptide or the V_H-C_H1 polypeptide.

a 29. A vector comprising a polynucleotide according to ^{Claim 13} ~~any one of claims~~
a ~~13 to 29~~.

20 30. A bacterial, yeast, insect or mammalian host cell transformed with a vector according to claim 29.

25 31. A method of producing a chimeric antibody conjugate which comprises culturing a host cell according to claim 30 under conditions enabling the expression of the conjugate and optionally recovering the conjugate.

30 32. A chimeric antibody conjugate produced by a method according to claim 31.

a 33. A method for detecting an antibody in a biological sample which
a involves comparing the level of detection obtained with the biological sample to the level of detection obtained with a positive control, wherein the
35 positive control comprises a chimeric antibody conjugate according to ^{Claim 1} ~~any one of claims 1 to 12~~.

34. A method according to claim 33 in which the biological sample is a human biological sample.

a 5 35. A method according to claim 33 ~~or claim 34~~ in which the antibodies to be detected are antibodies characteristic of a disease selected from dengue fever, japanese encephalitis, rubella, spotted fever, herpes infection, parvovirus infections, melioidosis, typhoid, leptospirosis, malaria, yellow fever, whooping cough, systemic candidiasis/thrush, chicken pox, shingles.
10 AIDS, hepatitis, liver cancer, cervical cancer, infectious mononucleosis, nasopharyngeal carcinoma, Ross River fever, brucella, exanthum subitum (sixth disease/roseola infantum), erythema infectiosum (fifth disease), Q fever, cold sores, genital herpes, spotted fever and scrub typhus.

a 15 36. A method according to ^{Claim 33} ~~any one of claims 33 to 35~~ in which the antibody is an IgM antibody.

a 37. A method according to ^{Claim 33} ~~any one of claims 33 to 35~~ in which the antibody is an IgG antibody.

20 38. A method according to ^{Claim 33} ~~any one of claims 33 to 35~~ in which the antibody is an IgA antibody.

25 39. A bifunctional molecule for use in labelling an antibody derived from a first species, the bifunctional molecule comprising a binding region which binds to the antibody of the first species or to one or more groups provided thereon, and a constant region derived from an antibody of a second species, the constant region comprising at least one C_H domain or an epitope thereof.

30 40. A bifunctional molecule according to claim 39 in which the binding and constant regions are separated by a linker molecule.

41. A bifunctional molecule according to claim 40 in which the linker molecule is a peptide of between 1 and 20 amino acids in length.

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42. A bifunctional molecule according to claim 41 in which the linker molecule is a peptide of between 2 and 5 amino acids in length.

a 43. A bifunctional molecule according to ^{Claim 39} ~~any one of claims 39 to 42~~ in which the binding region is not derived from an antibody.

a 44. A bifunctional molecule according to ^{Claim 39} ~~any one of claims 39 to 43~~ in which the binding region binds directly to the antibody derived from the first species.

10 45. A bifunctional molecule according to claim 44 in which the binding region is derived from a protein selected from the group consisting of, *Streptococcal* protein G, *Staphylococcal aureus* protein A and *Peptostreptococcus magnus* protein L.

15 46. A bifunctional molecule according to claim 45 in which the binding region comprises fragment B of *Staphylococcus aureus* protein A.

20 47. A bifunctional molecule according to claim 44 in which the binding region comprises a mouse Fc γ receptor or fragment thereof.

48. A bifunctional molecule according to claim 44 in which the binding region comprises a histidine rich glycoprotein.

a 25 49. A bifunctional molecule according to ^{Claim 39} ~~any one of claims 39 to 43~~ in which the binding region binds to one or more groups provided on the antibody of the first species.

30 50. A bifunctional molecule according to claim 49 in which the group(s) is a biotin molecule and the binding region comprises streptavidin or a fragment thereof.

a 51. A bifunctional molecule according to ^{Claim 39} ~~any one of claims 39 to 50~~ in which the antibody constant region is not a naturally occurring Fc fragment.

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52. A bifunctional molecule according to ^{Claim 39} ~~any one of claims 39 to 51~~ in which the constant region comprises one or more constant domains derived from an IgM antibody.

5 53. A bifunctional molecule according to claim 52 in which the constant region comprises one or more $C_H3\mu$ domains.

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54. A bifunctional molecule according to ^{Claim 39} ~~any one of claims 39 to 51~~ in which the constant region comprises one or more constant domains derived from an IgG antibody.

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55. A bifunctional molecule according to claim 54 in which the constant region comprises one or more $C_H3\gamma$ domains.

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15 56. A bifunctional molecule according to ^{Claim 39} ~~any one of claims 39 to 51~~ in which the constant region comprises one or more constant domains derived from an IgA antibody.

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20 57. A bifunctional molecule according to ^{Claim 39} ~~any one of claims 39 to 56~~ in which the antibody constant region comprises or consists of a non-naturally occurring combination of immunoglobulin C_H domains or epitopes thereof.

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25 58. A bifunctional molecule according to ^{Claim 39} ~~any one of claims 39 to 56~~ in which the antibody constant region comprises or consists of a single C_H domain.

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59. A bifunctional molecule according to ^{Claim 39} ~~any one of claims 39 to 58~~ in which the second species is a human.

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30 60. An isolated polynucleotide encoding a bifunctional molecule according to ^{Claim 39} ~~any one of claims 39 to 59~~.

61. A vector comprising a polynucleotide according to claim 60.

35 62. A bacterial, yeast, insect or mammalian host cell transformed with a vector according to claim 61.

63. A method of producing a bifunctional molecule which comprises culturing a host cell according to claim 62 under conditions enabling the expression of the bifunctional molecule and optionally recovering the
5 bifunctional molecule.

64. A bifunctional molecule produced by a method according to claim 63.

10 65. A complex formed between (i) an antibody or biologically active fragment thereof derived from a first species and (ii) a bifunctional molecule, the bifunctional molecule comprising a binding region which binds to the antibody of the first species or to one or more groups provided thereon, and a
15 constant region derived from an antibody of a second species, the constant region comprising at least one C_H domain or an epitope thereof.

66. A complex according to claim 65 in which the binding region has a K_D for the antibody of the first species, or a group provided thereon, of less than 10⁻⁶ M.
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67. A complex according to claim 66 in which the binding region has a K_D for the antibody of the first species, or a group provided thereon, of less than 10⁻⁸ M.

25 68. A complex according to ^{claim 65} ~~any one of claims 65 to 67~~ in which the bifunctional molecule binds directly to the antibody derived from the first species.

69. A complex according to claim 68 in which the binding region is
30 derived from a protein selected from the group consisting of, *Streptococcal* protein G, *Staphylococcal aureus* protein A and *Peptostreptococcus magnus* protein L.

70. A complex according to claim 69 in which the binding region
35 comprises fragment B of *Staphylococcus aureus* protein A.

71. A complex according to claim 68 in which the binding region comprises a mouse Fc γ receptor or fragment thereof.

5 72. A complex according to claim 68 in which the binding region comprises a histidine rich glycoprotein.

a 73. A complex according to any ^{Claim 65} ~~one of claims 65 to 67~~ in which the binding region binds to one or more groups provided on the antibody of the first species.

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74. A complex according to claim 73 in which the group(s) is a biotin molecule and the binding region comprises streptavidin or a fragment thereof.

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a 75. A complex according to any ^{Claim 65} ~~one of claims 65 to 74~~ in which the constant region comprises one or more constant domains derived from an IgM antibody.

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76. A complex according to claim 75 in which the constant region comprises one or more C_H3 μ domains.

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a 77. A complex according to any ^{Claim 65} ~~one of claims 65 to 74~~ in which the constant region comprises one or more constant domains derived from an IgG antibody.

78. A complex according to claim 77 in which the constant region comprises one or more C_H3 γ domains.

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a 79. A complex according to any ^{Claim 65} ~~one of claims 65 to 74~~ in which the constant region comprises one or more constant domains derived from an IgA antibody.

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a 80. A complex according to any ^{Claim 65} ~~one of claims 65 to 79~~ in which the antibody constant region comprises or consists of a non-naturally occurring combination of immunoglobulin C_H domains or epitopes thereof.

- a 81. A complex according to ^{Claim 65} ~~any one of claims 65 to 79~~ in which the antibody constant region comprises or consists of a single C_H domain.
- a 82. A complex according to ^{Claim 65} ~~any one of claims 65 to 81~~ in which the first
5 species is a rat or mouse.
- a 83. A complex according to ^{Claim 65} ~~any one of claims 65 to 82~~ in which the second species is a human.
- 10 84. A method for detecting an antibody in a biological sample which involves comparing the level of detection obtained with the biological sample to the level of detection obtained with a positive control, wherein the
a positive control comprises a complex according to ^{Claim 65} ~~any one of claims 65 to 83~~.
- 15 85. A method according to claim 84 in which the biological sample is a human biological sample.
- a 86. A method according to claim 84 ~~or claim 85~~ in which the antibodies to be detected are antibodies characteristic of a disease selected from dengue
20 fever, Japanese encephalitis, rubella, spotted fever, herpes infection, parvovirus infections, melioidosis, typhoid, leptospirosis, malaria, yellow fever, whooping cough, systemic candidiasis/thrush, chicken pox, shingles, AIDS, hepatitis, liver cancer, cervical cancer, infectious mononucleosis, nasopharyngeal carcinoma, Ross River fever, brucella, exanthum subitum
25 (sixth disease/roseola infantum), erythema infectiosum (fifth disease), Q fever, cold sores, genital herpes, spotted fever and scrub typhus.
- a 87. A method according to ^{Claim 84} ~~any one of claims 84 to 86~~ in which the antibody is an IgM antibody.
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- a 88. A method according to ^{Claim 84} ~~any one of claims 84 to 86~~ in which the antibody is an IgG antibody.
- a 89. A method according to ^{Claim 84} ~~any one of claims 84 to 86~~ in which the
35 antibody is an IgA antibody.